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Summary of FDCA Section 503A and H.R. 3204 "Drug Quality and Security Act"

- Applies only to human drugs
- **Section 503A of the FDCA from 1997 remains in effect (without the unconstitutional advertising provisions)**

Section 503A

- Under 503A, cGMP, adequate direction for use, and new drug provisions of FDCA **do not** apply if:
  - a sterile or non-sterile drug is compounded for an **identified individual patient and**
  - the compound is based on receipt of a valid prescription/order and
  - is compounded by a licensed pharmacist/physician. (Sec. 503A(a)(1))
- Pharmacist/physician may **compound in limited quantities before receipt** of a prescription for individual patient if, based on history of the pharmacist or physician receiving prescriptions for the drug product generated solely within established relationship:
  - between the pharmacist/physician and patient, or
  - between the pharmacist and other practitioner that writes the prescription order (503A(a)(2))
- Compounding using **bulk drug substances**
  - Must comply with USP/NF monograph (if they exist), and the USP chapter on compounding
  - If no monograph exists, then must be component of an approved drug
  - If neither of the above, then must appear on a list issued by Secretary through regulations (503A(b)(1)(A))
- Compounding using Ingredients **other than bulk substances**
  - Must comply with USP/NF if a monograph exists, and USP chapter on compounding (503A(b)(1)(B))
- **Drugs removed/withdrawn** from market as unsafe or not effective
  - Cannot compound if appear on list published by Secretary

- **Essentially a copy** of a commercially available drug
    - Cannot compound regularly or inordinate amounts (as defined by the Secretary)
    - Does not include a compounded drug for an identified individual, which produces in that patient a significant difference between compounded drug and commercially available drug (503A(b)(1)(D); 503A(b)(2))
- Drugs **presenting "demonstrable difficulties to compound"** that reasonably demonstrate an adverse effect on the safety and effectiveness of that product
    - Drugs impermissible to compound; identified by Secretary by regulation (503A(b)(3)(A))
- **A drug may be compounded only if:**
    - The drug is compounded in a state that has entered into a memorandum of understanding (MOU) with Secretary addressing the distribution of inordinate amounts interstate; providing for appropriate investigation of complaints by state agency relating to compounded products distributed outside of the state that compounded the drug product, ***or***
    - If the state has ***not*** entered into a MOU and the pharmacist/physician distributes/causes to be distributed compounded drug products *outside of the state,* in quantities that **do not exceed 5%** of total prescription orders dispensed or distributed by such pharmacy/physician.
    - The Secretary shall develop, in consultation with NABP, a standard MOU.

Section 503B: "Outsourcing Facilities"

- **Effective upon date of enactment (when signed by President)**
- New drug (505); directions for use (502(f)(1)); track/trace (582/new) not apply
- **Not** exempt from cGMP
- **Voluntary election** to register as outsourcing facility
- Outsourcing facility acts under direct supervision of licensed pharmacist
- **Not required** to be a pharmacy
- **"Outsourcing facility" defined as:**
    - Facility at **one geographic location** that:
        (1) is engaged in the compounding of **sterile products;**
        (2) has **elected to register** as an outsourcing facility; and
        (3) complies with the requirements of section 503B.
    - **May or may not obtain prescriptions for identified individual patients**

- May **compound using bulk substances, *if***:
  - Bulk substance **appears on list established by Secretary** addressing clinical need (after notice and comment rulemaking); **or**
  - **Appears on drug shortage list** in effect at time of compounding, distribution, and dispensing; ***and***
  - **If** USP/NF monograph (or other compendium recognized by Secretary) exists; then bulk substances each comply with it
  - Manufactured in FDA registered establishment
  - Accompanied by a certificate of analysis
- May compound using **ingredients other than bulk substances**
  - If comply with USP/NF/other compendium recognized by Secretary
- Drugs **withdrawn/removed for safety/effectiveness**
  - May not appear on list published by Secretary re drugs withdrawn/removed for safety/ineffectiveness
- **Essentially copies** of approved drugs
  - May not be "essentially a copy of one or more approved drugs," unless a change produces for individual a clinical difference (specifically defined in the legislation)
- **Demonstrable difficulties** for compounding
  - Drug may not be on list by Secretary re present demonstrable difficulties for compounding. (Note: may be compounded in accordance with conditions established by Secretary)
- Drugs subject to **elements to assure safe use/REMS**
  - Must demonstrate to Secretary **prior to** compounding that will utilize controls **comparable to applicable REMS**.[1]
- **Wholesaling prohibited**
- **Labeling:** requirements include:
  - Identification that it is a compounded drug; name, address, and phone number of outsourcing facility; lot/batch number; established drug name; dosage form/strength; volume; date compounded; expiration date; NDC; "not for resale:" list of active/inactive ingredients; FDA adverse event contact information; directions for use.
- **Registration requirements** - Annual; must indicate whether intend to compound drugs on shortage list during subsequent year
- **Drug Reporting Requirements**
  - Every six months must submit an electronic, confidential report to Secretary identifying drugs compounded during prior 6-month period, including:

[1] REMS/similar provision inapplicable to compounders under 503A

  - active ingredient(s); NDC number; source of bulk active ingredient; strength of active ingredient per unit; dosage form; route of administration; package description; number od individual units produced. (In a form and manner that Secretary may prescribe by regulation.
- **Inspections**
  - Subject to inspection pursuant to FDCA 704, and are not eligible for the pharmacy exemption under 704(a)(2)(A). Inspections may occur on a risk-based schedule
- **Adverse event reports**
  - Must submit adverse event reports
- **Definitions**
  - Defines "compounding", "essentially a copy of an approved drug," "approved drug," "outsourcing facility," "sterile drug"
- **Fees**
  - Must pay annual registration fees
  - Secretary may assess annual establishment fee ($15,000), reinspection fee ($15,000) for each inspection in a given fiscal year, subject to adjustments, including small business adjustment
  - Exception for small businesses – Gross annual sales of $1,000,000 or less; fee would be approximately 1/3
  - Not registered until pay fee
  - Drugs manufactured/prepared/compounded when fee not paid deemed misbranded
  - Must report annually to Congress on fees, entities paying fees, inspections, and staff
- **Penalties**
  - "Prohibited acts" for compounded drugs now include reselling, intentional falsification of a prescription, failure to report adverse events
  - FDCA Section 502 amended to include prohibition re: "If the advertising or promotion of a compounded drug is false or misleading in any particular"
- **Enhanced communications concerning Compounding Pharmacies** (Section 105)
  - In manner specified by Secretary (in consultation with NABP) Secretary shall receive submissions from state boards of pharmacy: (1) describing "actions" taken against compounding pharmacies; or (2) expressing concerns that compounding pharmacy may be in violation of 503A. "Actions include warning letters, sanctions, penalties for state violations, suspension or revocation or license; recalls due to quality or purity concerns.

  - Secretary shall immediately notify state boards of pharmacy when (1) it receives a submission from a state; (3) it makes a determination a pharmacy is acting contrary to 503A.
- **GAO Study** – Within 36 months after enactment, FDA shall submit a report to Congress on compounding and adequacy of federal and state efforts to assure safety of compounded drugs.